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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,766	07/12/2001	Avi Ashkenazi	10466/70	4054
35489	7590	01/21/2004	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 275 MIDDLEFIELD ROAD MENLO PARK, CO 94025-3506			KEMMERER, ELIZABETH	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/904,766

Applicant(s)

ASHKENAZI ET AL.

Examiner

Elizabeth C. Kemmerer, Ph.D.

Art Unit

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-- **Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 and 23 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-46 and 49-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-46 and 49-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10/17/03. 6) ☐ Other: _____

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DETAILED ACTION

Status of Application, Amendments, And/Or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 October 2003 has been entered. The declarations of Drs. Goddard, Gurney and Wood filed under 37 CFR 1.132 have been received (17 October 2003) and entered into the record.

The preliminary amendments received 17 October 2003 and 23 October 2003 have been entered in full. Claims 1-43, 47 and 48 are canceled. Claims 44-46 and 49-52 are under examination.

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1646, Examiner Elizabeth C. Kemmerer, Ph.D.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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Withdrawn Objections And/Or Rejections; Resolved Issues

The issue regarding enablement of variants, as set forth at p. 5 of the previous Office Action (Item B; Paper No. 20, 02 June 2003) has been resolved due to the amended claims submitted in the amendment received 17 October 2003.

The rejection of claims 39-43 and 50-51 under 35 U.S.C. § 112, first paragraph, regarding inadequate written description, as set forth at p. 6 of the previous Office Action (Paper No. 20, 02 June 2003) is *withdrawn* in view of the amended claims submitted in the amendment received 17 October 2003.

The alternative rejection of claims 39-46 and 49-51 under 35 U.S.C. § 102(a) as being anticipated by Wood et al. (WO 99/14328) as set forth at p. 7 of the previous Office Action (Paper No. 20, 02 June 2003) is *withdrawn* in view of the Wood, Goddard and Gurney declarations submitted under 37 CFR 1.132 received 17 October 2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 17 October 2003 has been received. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Correction of Inventorship

In view of the papers filed 17 October 2003, the inventorship in this nonprovisional application has been changed by the deletion of Inventors Ashkenazi,

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Botstein, Desnoyers, Eaton, Ferrara, Filvaroff, Fong, Gao, Gerber, Gerritsen, Grimaldi, Hillan, Kljavin, Mather, Pan, Paoni, Stewart, Tumas and Williams.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

35 U.S.C. §§ 101 and 112, First Paragraph

Claims 44-46 and 49-52 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by a credible, specific and substantial asserted utility or a well established utility.

Claims 44-46 and 49-52 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would clearly not know how to use the claimed invention.

The basis for these rejections is set forth at pp. 3-5 of the previous Office Action (Paper No. 20, 02 June 2003).

Applicant's arguments submitted in the responses received 17 October 2003 and 23 October 2003 have been fully considered but are not found to be persuasive for the following reasons. The Goddard declaration under 37 CFR 1.132 filed 21 February 2003 is insufficient to overcome the rejection of claims 39-43 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth in the last Office action for the following reasons.

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Applicant discusses the gene amplification assay, and refers to the Goddard declaration filed under 37 CFR 1.132 (received 21 February 2003) to address the concerns regarding the assay raised in the previous Office Actions. Applicant also refers to the Ashkenazi declaration filed under 37 CFR 1.132; however, Applicant is advised that this declaration is not of record in the instant application. In the interest of compact prosecution, it will be assumed that the Ashkenazi declaration referred to in the amendment is the same as that filed in related application 09/902,713 on 16 October 2003. These arguments and declaration, including publications using the same assay, have been very helpful in addressing the questions raised in the previous Office Actions. It is now conceded that the gene amplification assay provides a patentable utility for the PRO269 nucleic acid. However, the instant application has claims directed to PRO269 polypeptides. Applicant argues that the utility of the PRO269 nucleic acid carries over to the polypeptide and antibody claims. Specifically, Applicant argues that there is an assumption of utility unless a reason for one skilled in the art to question the objective truth of the statement of utility or its scope can be established. Applicant cites case law in support of this assertion. Applicant urges that a *prima facie* case of lack of utility has not been established. Applicant argues that the examiner has not established whether or not a lack of correlation between gene copy number and protein levels is an exception to the rule, or is the rule. Applicant asserts that the working hypothesis among those skilled in the art is that, if a gene is amplified in cancer, the encoded protein is likely to be expressed at an elevated level. This has been carefully considered but is not found to be persuasive. No evidence has been submitted that it is

the norm rather than the exception that protein levels are increased when gene amplification occurs in cancer. Indeed, evidence exists in the art that there is not always such a correlation, and thus the skilled artisan would not assume it is so, but would perform the experiment to verify it. Pennica et al. (1998, PNAS USA 95:14717-14722) disclose that,

"An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left-hand column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors". See also Konopka (Proc. Natl. Acad. Sci. (1986) 83:4049-4052), who state that

"Protein expression is not related to amplification of the *abl* gene but to variation in the level of *bcr-abl* mRNA produced from a single Ph1 template" (see abstract).

Finally, even if gene amplification correlates with increased transcription, it does not always follow that protein levels are also amplified. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA

transcript (p. 1863, second paragraph, and Figure 1). Therefore, the art indicates that it is not the norm that gene amplification, or even increased transcription, results in increased protein levels. Finally, Applicant refers to the Ashkenazi declaration which is not of record in the instant application. Applicant also provides a quote from the Ashkenazi declaration, which asserts that if the protein levels do not increase as a result of gene amplification, it is also useful because it can serve to better diagnose the cancer. This has been fully considered but is not found to be sufficient to withdraw the rejection, since there is no indication that the PRO269 protein levels increase or stay the same. Further research would be needed to determine PRO269 protein levels in cancers showing gene amplification of PRO269 gene.

Therefore, the asserted utility is not substantial, as the real-world use has not been established. Thus, the proposed use of the PRO269 proteins are simply starting points for further research and investigation into potential practical uses of the proteins and antibodies. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Therefore, the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, are maintained.

Priority

Applicant's comments, received 17 October 2003, regarding the priority claimed in the instant application are acknowledged. Applicant maintains that the instant claims are entitled to an effective filing date of 11 February 2000. However, for the reasons set forth above in the rejection of the claims for lack of utility and enablement, the effective filing date for the instant claims remains determined to be 12 July 2001.

35 U.S.C. § 102

Claims 44-46 and 49-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Wood et al. (WO 99/14328), as set forth at p. 7 of the previous Office Action (Paper No. 20, 02 June 2003).

In the amendments received 17 October 2003 and 23 October 2003, Applicant argues that the reference is unavailable under 35 U.S.C. § 102(b) as prior art because Applicant asserts that the claims are entitled to benefit of the 11 February 2000 filing date. Applicant's arguments have been carefully considered but are not found to be persuasive. For the reasons set forth above, the filing date of the instant claims is determined to be 12 July 2001. Wood et al. is thus properly applied under 35 U.S.C. § 102(b).

Claims 44-46 and 49-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al. (WO 00/11015), as set forth at p. 8 of the previous Office Action (Paper No. 20, 02 June 2003).

In the amendments received 17 October 2003 and 23 October 2003, Applicant argues that the reference is unavailable under 35 U.S.C. § 102(b) as prior art because Applicant asserts that the claims are entitled to benefit of the 11 February 2000 filing date. Applicant's arguments have been carefully considered but are not found to be persuasive. For the reasons set forth above, the filing date of the instant claims is determined to be 12 July 2001. Valenzuela et al. is thus properly applied under 35 U.S.C. § 102(b).

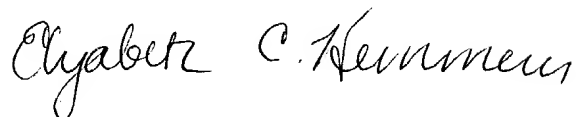
Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER